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Diastereoselective Addition of Allylzinc Bromide to Imines Derived from (*R*)-Phenylglycine Amide

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General. Reagents were purchased from Aldrich Chemical Company and were used without further purification. Crotyl bromide was purchased from Fluka. (*R*)-Phenylglycine amide was provided by DSM (Geleen, The Netherlands). Commercial grade THF was used. Zinc-wool was cut prior to use. NMR spectra were recorded on either a Varian VXR-300 spectrometer (300 MHz) or a Varian Gemini Spectrometer (200 MHz). Chemical shifts are denoted in ppm and were referenced to residual solvent. Melting points (uncorrected) were determined on a Mettler FP-2 melting point apparatus equipped with a Mettler FP-21 microscope. HPLC analysis was performed on a HP1100 equipped with a Chiralpak or Crownpak analytical column.

Typical procedure for the synthesis of (*R*) -phenylglycine amide-imines 2-11. To a suspension of (*R*)-phenylglycine amide (200 mmol, 30.0 g) in CH_2Cl_2 (200 mL) at ambient temperature was added benzaldehyde (200 mmol, 21.2 g, 20.3 mL). The reaction mixture was stirred overnight. at room temperature. $MgSO_4$ (10 g) was added and the reaction mixture was filtered. Evaporation of the solvent yields **2** as a colorless solid, which was recrystallized once from acetone/hexane (colorless crystals, 84%). m.p. 138-139 ^oC. ^1H NMR (200MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.80 (m, 2H), 7.25-7.51 (m, 10H), 7.03 (bs, 1H), 5.84 (bs, 1H), 4.99 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 160.79, 129.04, 126.25, 126.03, 125.45, 124.81, 74.50. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.53; H, 5.99; N, 11.78.

(3). To a suspension of (*R*)-phenylglycine amide (15.0 g, 100 mmol) in $CHCl_3$, was added piperonal (15.0 g, 100 mmol) and a catalytic amount of *p*-$TolSO_3H$ (0.3 g). The mixture was refluxed for 2 hours. $MgSO_4$ was added and the mixture was filtered. The filtrate was evaporated and the residue was crystallized from Et_2O. (colorless powder, 85 %) m.p. 138-139 ^oC. ^1H NMR (200 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.26-7.49 (m, 6H), 7.11-7.16 (m, 1H), 7.00 (bs, 1H), 6.81-6.86 (m, 1H), 6.02 (s, 1H), 6.03 (s, 1H), 5.86 (bs, 1H), 4.94, (s, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ 173.19, 160.79, 149.04, 146.56, 138.03, 128.78, 127.20, 126.39, 125.79, 123.94, 106.64, 104.97, 100.14, 75.24. Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.08; H, 5.00; N, 9.92. Found: C, 67.74; H, 5.07; N, 9.97.

(4). (pale yellow powder, 90%) m.p. 139-140 ^oC. ^1H NMR (200 MHz, DMSO-d_6) δ 9.5 (bs, 1H), 8.25 (s, 1H), 7.69 (d, J = 8.57 Hz, 2H), 7.20-7.38 (m, 5H), 6.80 (d, J = 8.55 Hz, 2H), 4.73 (s, 1H), 3.34 (bs, 2H). ^{13}C NMR (50 MHz, DMSO-d_6): δ 183.25, 172.08, 163.12, 160.88, 159.24, 139.62, 129.28, 127.22, 126.30, 126.06, 114.40, 75.63. Anal. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.02; H, 5.53; N, 10.69.

(5). (colorless crystals, 87%) m.p. 140-141 ^oC. ^1H NMR (200MHz, $CDCl_3$): 8.73 (s, 1H), 7.59 (d, J = 3.17 Hz, 1H), 7.46-7.51 (m, 2H), 7.26-7.39 (m, 3H), 6.97-7.03 (m, 2H), 6.83-6.88 (m, 1H), 4.99 (s, 1H), 3.83 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.14, 152.29, 152.10, 138.11, 127.15, 126.30, 125.75, 122.88, 117.37, 111.16, 109.78, 75.89, 54.62, 54.35. Anal. Calcd for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.44; H, 6.14; N, 9.26.

(6). (colorless crystals, 90%). m.p. 113-114 ^oC. ^1H NMR (200MHz, $CDCl_3$) δ 8.93 (d, J = 1.46 Hz, 1H), 8.66 (d, J = 3.17 Hz, 1H), 8.33 (s, 1H), 8.14 (m, 1H), 7.26-7.47 (m, 6H), 6.9 (bs, 1H), 6.4 (bs, 1H), 5.00 (s, 1H). ^{13}C NMR (50 MHz, DMSO-d_6): δ 171.34, 159.42, 150.69, 148.99, 139.03, 134.13, 130.11, 127.31, 126.35, 122.78, 75.84. Anal. Calcd for $C_{14}H_{13}N_3O$: C, 70.28; H, 5.48; N, 17.56. Found: C, 70.01; H, 5.54; N, 17.49.

(7). (colorless crystals, 89 %) m.p. 144-145 ^oC. ^1H NMR (200MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.26-7.56 (m, 6H), 7.04 (bs, 1H), 6.82-6.84 (m, 1H), 6.48-6.51 (m, 1H), 6.19 (bs, 1H), 4.92 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 169.88, 149.91, 149.57, 143.99, 137.67, 127.28, 126.52, 125.96, 114.45, 110.49, 75.64. Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 67.48; H, 5.29; N, 12.32.

(8). (pale yellow crystals, 80 %) m.p. 135-136 ^oC. ^1H NMR (200MHz, $CDCl_3$): δ 8.37 (s, 1H), 7.28-7.49 (m, 7H), 7.07-7.11 (m, 1H), 7.02 (bs, 1H), 5.63 (bs, 1H), 4.96 (s, 1H). ^{13}C NMR (50MHz,$CDCl_3$):δ 172.81, 154.71, 140.12, 137.69, 130.53, 128.5, 127.24, 126.47, 126.19, 125.87, 74.72. Anal. Calcd for $C_{13}H_{12}N_2OS$: C, 63.91; H, 4.95; N, 11.47. Found: C, 63.76; H, 4.97; N, 11.30.

(9). (pale yellow plates, 95%) ^{1}H-NMR (300MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.34 (d, 2H), 7.21-7.30 (m, 3H), 6.90 (bs, 1H), 5.90 (bs, 1H), 4.66 (s, 1H), 1.05 (s, 9H). ^{13}C-NMR (50MHz, $CDCl_3$) δ 174.77, 174.49, 139.41, 128.53, 127.67, 126.88, 76.33, 26.64. MS (CI): m/z=219 (M+1).

(10). (colorless crystals, 95%) m.p. 91-92 °C. ^{1}H NMR (200MHz, $CDCl_3$): δ 7.60 (d, *J* = 4.39, 1H), 7.21-7.37 (m, 5H), 6.90 (bs, 1H), 5.86 (bs, 1H), 4.67 (s, 1H), 2.46 (m, 1H), 1.06 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.36, 170.92, 137.93, 127.09, 126.23, 125.58, 75.23, 32.71, 17.43, 17.37. Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.89; N, 13.71. Found: C, 70.07; H, 7.85; N, 13.62.

(11). (colorless powder, 86%) m.p. 84-85 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.74 (t, *J* = 5.1 Hz, 1H), 7.26-7.43 (m, 5H), 6.90 (bs, 1H), 5.68 (bs, 1H), 4.74 (s, 1H), 2.21 (m, 2H), 1.99 (m, 1H), 0.94 (m, 6H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ 165.34, 126.14, 125.28, 124.63, 74.82, 42.44, 23.55, 20.03. Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.16; H, 8.25; N, 12.98.

Typical procedure for the allylation of (*R*)-phenylglycine amide-imines. A solution of allylzinc bromide (1.5 eq) was prepared by adding allylbromide (438 mmol, 38.5 mL) to finely cut zinc-wool (438 mmol, 28.6 g) in THF (250 mL). The solution of allylzinc bromide was cooled to room temperature and was added dropwise to a solution of **2** (292 mmol, 70 g) in THF (150 mL) at 0°C. The reaction mixture was warmed to room temperature and was poured into water (500 mL). EtOAc (200 mL) was added and the mixture was stirred vigorously. After filtration through a glass filter, the organic phase was separated and the water layer was extracted with EtOAc (2 x 100 mL). The combined organic layers were dried on $MgSO_4$ and concentrated to give **12** as a colorless oil that crystallized on standing (colorless crystals, 93%). m.p. 89-90 °C. ^{1}H NMR (200MHz, $CDCl_3$): δ 7.15-7.31 (m, 10H), 7.05 (bs, 1H), 6.22 (bs, 1H), 5.67-5.78 (m, 1H), 5.01-5.09 (m, 2H), 3.95 (s, 1H), 3.68 (t, *J* = 7.0 Hz, 1H), 2.40 (dd, *J* = 7.0 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.57, 140.33, 137.05, 132.60, 126.33, 126.14, 125.56, 124.97, 124.80, 124.59, 115.32, 61.91, 59.12, 40.16. Anal. Calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 76.95; H, 7.22; N, 9.92.

(13). (colorless crystals, 81 %) m.p. 110-111 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.21-7.23 (m, 5H), 6.93 (bs, 1H), 6.61-6.72 (m, 3H), 5.90 (s, 2H), 5.64-5.74 (bm, 2H), 5.00-5.07 (m, 2H), 3.99 (s, 1H), 3.60 (t, *J* = 6.96 Hz, 1H), 2.34-2.39 (dd, *J* = 6.96 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.24, 146.46, 145.30, 137.87, 135.21, 133.47, 127.31, 126.56, 125.72, 119.03, 116.25, 106.64, 105.47, 99.51, 59.92, 41.12. Anal. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.21; N, 8.64. Found: C, 70.28; H, 6.33; N, 8.59.

(14). (colorless solid, 90%) m.p. 158-159 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 9.20 (bs, 1H), 7.54 (s, 1H), 7.22-7.29 (m, 5H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 5.70 (m, 1H), 5.00 (m, 2H), 3.87 (s, 1H), 3.50 (m, 1H), 2.25 (m, 2H). ^{13}C NMR (50 MHz, DMSO- d_6) δ 173.2, 155.2, 139.4, 134.8, 132.6, 127.2, 127.0, 125.9, 115.9, 113.9, 61.5, 58.7, 41.9. Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 72.90; H, 6.84; N, 9.45.

(15). (yellow crystals, 93%) m.p. 121-122 °C. ^{1}H NMR (200MHz, $CDCl_3$): δ 7.48 (bs, 1H), 7.12-7.23 (m, 5H), 5.73-5.85 (m, 2H), 4.99-5.07 (m, 2H), 3.95 (s, 1H), 3.85 (t, *J* = 6.96 Hz, 1H), 3.86 (s, 3H), 3.60 (s, 3H), 2.40-2.45 (dd, *J* = 6.96 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 198.91, 174.71, 152.02, 150.14, 138.30, 134.39, 129.75, 127.21, 126.40, 125.75, 115.72, 113.14, 110.91, 110.28, 63.36, 57.30, 54.15, 54.05, 39.02. Anal. Calcd for $C_{20}H_{24}N_2O_3$: C, 70.57; H, 7.11; N, 8.23. Found: C, 70.38; H, 7.16; N, 8.13.

(16). (pale yellow powder, 43 %). m.p. 96-97 °C. ^{1}H NMR (200MHz, $CDCl_3$) δ 8.58 (s, 2H), 7.77 (d, *J* = 7.69 Hz, 1H), 7.36 (m, 1H), 7.15 (m, 5H), 6.41 (bs, 1H), 5.45-5.65 (m, 2H), 5.00 (m, 2H), 3.89 (s, 1H), 3.79 (t, *J* = 7.04 Hz, 1H), 2.38 (m, 2H). ^{13}C NMR (50 MHz, DMSO-d_6): δ 172.91, 147.64, 147.00, 138.99, 138.34, 134.94, 133.81, 127.06, 125.92, 122.97, 116.72, 61.72, 56.97, 41.27. Calcd for $C_{17}H_{19}N_3O$: C, 72.57; H, 6.81; N, 14.93. Found: C, 72.50; H, 6.81; N, 15.1.

(17). (colorless solid, 88 %). m.p. 77-78 °C. ^{1}H NMR (200MHz, $CDCl_3$) δ 7.21-7.35 (m, 6H), 6.30-6.33 (m, 1H), 6.17-6.19 (m, 1H), 6.14 (bs, 1H), 5.69-5.90 (m, 1H), 5.07-5.17 (m, 2H), 4.11 (s, 1H), 3.74 (t, *J* = 6.84 Hz, 1H), 2.47-2.55 (m,

2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 174.56, 153.57, 140.38, 137.87, 133.08, 127.28, 126.56, 126.34, 125.87, 116.47, 108.55, 105.89, 63.09, 53.46, 37.99.

(18). (yellow crystals, 90%) m.p. 62-63 °C. ^{1}H NMR (200MHz, $CDCl_3$): δ 7.22-7.30 (m, 6H), 6.89-6.97 (bm, 3H), 5.75-5.89 (bm, 2H), 5.08-5.09 (m, 2H), 4.19 (s, 1H), 4.02 (t, *J* = 6.8 Hz, 1H), 2.50-2.58 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 174.02, 145.95, 137.67, 132.99, 127.28, 126.56, 125.83, 125.03, 123.57, 122.82, 116.66, 62.75, 55.53, 41.63. Anal. Calcd for $C_{16}H_{18}N_2OS$: C, 67.10; H, 6.34; N, 9.78. Found: C, 66.95; H, 6.32; N, 9.73.

(19) (yellow oil, 89%) ^{1}H-NMR (300MHz, $CDCl_3$) δ 7.18-7.26 (m, 5H), 6.85 (bs, 1H), 6.77 (bs, 1H), 5.75-5.89 (m, 1H), 4.95-5.06 (m, 2H), 4.28 (s, 1H), 2.33-2.38 (m, 1H), 2.15-2.18 (m, 1H), 1.95-2.06 (m, 1H), 0.76 (s, 9H). ^{13}C-NMR (50MHz, $CDCl_3$) δ 176.24, 139.44, 137.76, 128.47, 127.80, 127.75, 65.89, 63.89, 36.09, 35.22, 26.91. MS (CI): m/z=261 (M+1).

(20). (yellowish oil, 77 %). ^{1}H NMR (200MHz, $CDCl_3$): δ 7.20-7.34 (m, 6H), 6.02 (bs, 1H), 5.76 (m, 1H), 5.07 (d, *J* = 10.6 Hz, 1H), 5.03 (s, 1H), 4.25 (s, 1H), 2.37 (m, 1H), 2.17 (m, 1H), 1.87 (m, 2H), 0.85 (d, *J* = 6.6 Hz, 3H), 0.72 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 174.02, 137.24, 134.00, 126.32, 125.54, 124.96, 114.74, 62.39, 58.53, 32.23, 26.79, 16.45, 14.53. Anal. Calcd for $C_{15}H_{22}N_2O$: C, 73.13; H, 9.00; N, 11.37. Found: C, 73.13; H, 9.23; N, 11.16.

(21). (pale yellow solid, 94%) m.p. 56-57 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.18-7.39 (m, 6H), 5.88 (bm, 2H), 5.04-5.14 (m, 2H), 4.28 (s, 1H), 2.58 (m, 1H), 2.16 (m, 2H), 1.60 (m, 2H), 1.22 (m, 2H), 0.80 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.9, 138.3, 133.79, 127.3, 126.5, 125.9, 116.1, 63.3, 52.14, 42.5, 37.4, 23.3, 21.3, 21.2. Anal. Calcd for $C_{16}H_{24}N_2O$: C, 73.81; H, 9.29; N, 10.76. Found: C, 73.81; H, 9.43; N, 10.67.

(22). A solution of crotylzinc bromide (1.5 eq) was prepared by adding crotylbromide (62.6 mmol, 6.4 mL) to finely cut zinc-wool (62.6 mmol, 4.0 g) in THF (50 mL). The solution of crotylzinc bromide was cooled to room temperature and was added dropwise to a solution of **2** (41.7 mmol, 10 g) in THF (30 mL) at 0°C. The reaction mixture was warmed to room temperature and was poured into water (100 mL). EtOAc (30 mL) was added and the mixture was stirred vigorously. After filtration through a glass filter, the organic phase was separated and the water layer was extracted with EtOAc (2 x 30 mL). The combined organic phase was dried over $MgSO_4$ and concentrated to give **22**. (orange oil, 98%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.99-7.29 (m, 2x10H), 6.69 (bs, 1H), 6.44 (bs, 1H), 5.72-5.84 (m, 1H), 4.46-5.58 (m, 1H), 4.98-5.15 (m, 2x2H), 3.97 (s, 1H), 3.89 (s, 1H), 3.70 (d, *J* = 5.13 Hz, 1H), 3.36 (d, *J* = 8.42 Hz, 1H), 2.41-2.65 (m, 1H), 2.31-2.41 (m, 1H), 0.92 (d, *J* = 6.95 Hz, 3H), 0.78 (d, *J* = 6.59 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.5, 175.2, 139.9, 139.7, 138.0, 137.5, 136.9, 127.6, 127.3, 127.0, 126.8, 126.7, 126.7, 126.3, 126.2, 126.1, 125.8, 115.3, 114.6, 65.3, 64.9, 62.6, 62.5, 43.2, 42.2, 16.3, 15.0.

(23). A solution of methallylzinc bromide (1.5 eq) was prepared by adding methallylbromide (62.6 mmol, 6.3 mL) to finely cut zinc-wool (62.6 mmol, 4.0 g) in THF (50 mL). The solution of methallylzinc bromide was cooled to room temperature and was added dropwise to a solution of **2** (41.7 mmol, 10 g) in THF (30 mL) at 0°C. The reaction mixture was warmed to room temperature and was poured into water (100 mL). EtOAc (30 mL) was added and the mixture was stirred vigorously. After filtration through a glass filter, the organic phase was separated and the water layer was extracted with EtOAc (2 x 30 mL). The combined organic layers were dried over $MgSO_4$ and concentrated to give **23** that can be crystallized from Et_2O (colorless solid, 98%). m.p. 104-109 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.14-7.30 (m, 10H), 6.95 (bs, 1H), 5.76 (bs, 1H), 4.80 (s, 1H), 4.73 (s, 1H), 4.00 (s, 1H), 3.75-3.80 (m, 1H), 2.27-2.43 (m, 2H), 1.72 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.1, 140.7, 140.5, 136.9, 127.4, 127.2, 126.8, 126.2, 125.9, 125.7, 112.4, 63.7, 62.5, 44.9, 21.1.

Typical procedure for the catalytic hydrogenation of (*R*)-phenylglycine amide-homoallylamines. Homoallylamine **12** (15.0 mmol, 4.2 g) was dissolved in MeOH (100 mL). Water (10 mL), acetic acid (2.5 mL), and Pd(10%)/C (0.6 gram) were added successively. The mixture was shaken under an atmosphere of H_2 (30 psi) for 18 hrs at room temperature. The MeOH was evaporated under reduced pressure. The residue was diluted with water (50 mL) and

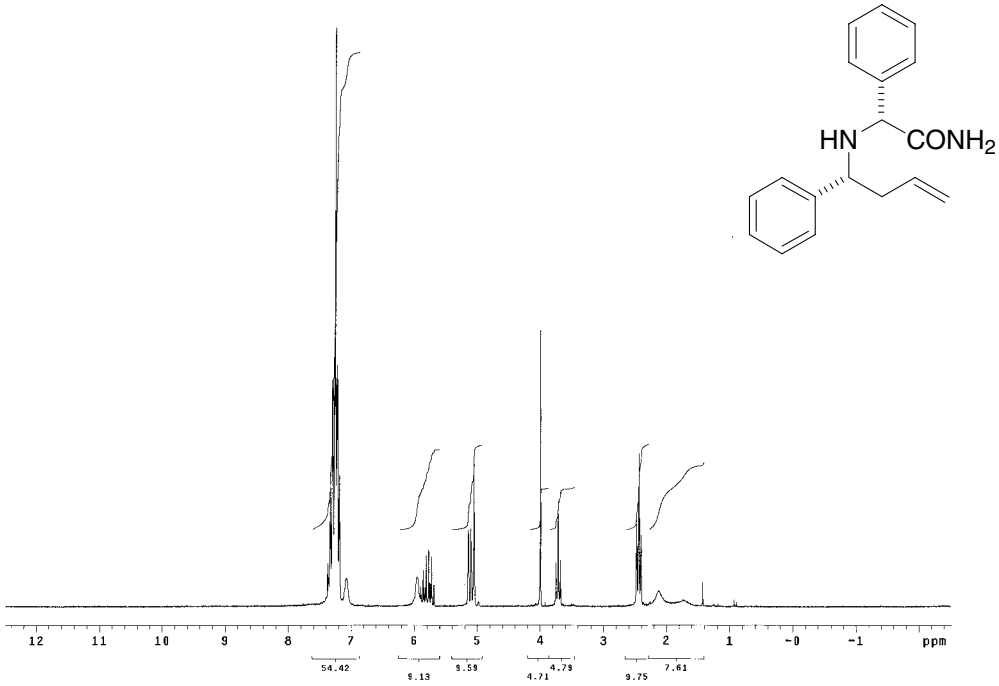
was adjusted to pH = 10 with 10 % NaOH. The water phase was extracted with CH_2Cl_2 (3 x 40 mL). The combined organic phase was dried on $MgSO_4$ and filtered. After evaporation of the CH_2Cl_2, pentane was added to the residue. Filtration through a glass filter yields crystalline phenylacetamide (0.8 g, 41%). Evaporation of the pentane left *(R)*-**24** as a colorless oil that slowly solidified on standing (1.1 g, 49%). $[\alpha]^{27}_{589}$ +18.3 (*c* = 1.06, $CHCl_3$). ^{1}H NMR 200MHz, $CDCl_3$): δ 7.20-7.34 (m, 5H), 3.89 (t, *J* = 6.84 Hz, 1H), 1.97 (bs, 2H), 1.60-1.69 (m, 2H), 1.21-1.36 (m, 2H), 0.93 (t, *J* = 7.08 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 141.21, 126.95, 125.81, 125.33, 53.85, 37.93, 17.81, 12.41.

(R)-**25** (colorless oil, 64%). $[\alpha]^{23}_{589}$ +17.0 (*c* = 0.99, $CHCl_3$). ^{1}H NMR 200MHz, $CDCl_3$): δ 2.38-2.44 (m, 1H), 0.85-1.40 (m, 8H), 0.74-0.84 (m, 9H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 54.5, 35.4, 31.6, 18.0, 17.5, 15.3, 12.5.

(R)-**26** (colorless oil, 88 %). $[\alpha]^{27}_{589}$ +10.9 (*c* = 1.01, $CHCl_3$). ^{1}H NMR (200MHz, $CDCl_3$): δ 6.83 (s, 1H), 6.74 (s, 2H), 5.92 (s, 2H), 3.80 (bs, 1H), 1.58-1.63 (bm, 2H), 1.18-1.26 (bm, 2H), 0.89 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 146.08, 144.67, 139.35, 117.85, 106.32, 105.00, 99.22, 54.22, 40.30, 18.15, 12.44.

Typical procedure for the non-reductive auxiliary removal (retro-Strecker method). To CH_2Cl_2 (600 mL), cooled with an ice bath, was added DMF (144 mmol, 10.6 g, 11.2 mL). Oxalylchloride (144 mmol, 18.5 g, 12.7 mL) was added dropwise. After the formation of gas (CO and CO_2) had ceased, a solution of amide **20** (97.6 mmol, 24.0 g) in CH_2Cl_2 (100 mL) was added dropwise in 10 minutes. Triethylamine (97.5 mmol, 9.8 g, 13.48 mL) was added dropwise in 5 minutes turning the reaction mixture orange-red. The reaction was stirred at room temperature for 30 minutes. Water (300 mL) was added and the organic phase was separated. The aqueous layer was washed with CH_2Cl_2 (100 mL) additionally. The organic layer was dried over Na_2SO_4 and concentrated to give the crude nitrile **28** (22.0 g, 95.6 mmol, 98%) as an orange oil. The crude nitrile (7.4 g; 33 mmol) was dissolved in ethanol (150 mL) and K_2CO_3 (8.97 g; 65 mmol; 2 eq.) was added. The reaction mixture was refluxed for 2 hours. The ethanol was evaporated and the residue was taken up in water/CH_2Cl_2. The organic phase was separated and dried over Na_2SO_4. Evaporation of the solvent gives the crude imine **30** (6.2 g, 30.8 mmol, 93%) as the only product. ^{1}H NMR (200MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.68-7.71 (m, 2H), 7.27-7.37 (m, 3H), 5.61-5.70 (m, 1H), 4.91-4.99 (m, 2H), 2.81-2.87 (m, 1H), 2.33-2.41 (m, 2H), 1.82-1.89 (m, 1H), 0.86-0.91 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 157.99, 135.01, 134.90, 128.74, 126.96, 126.65, 114.87, 75.79, 36.55, 31.14, 18.32, 17.11. MS (EI) [*m/e*, %]: 201 [M^+, 4.3]; 160[M^+-C_3H_5, 100]. Imine **30** (2.0 g, 9.94 mmol) was dissolved in a 50% aqueous THF. 3 equivalents of $NH_2OH.HCl$ (2.08 g, 29.8 mmol) were added and the reaction mixture was stirred overnight at ambient temperature. The THF was evaporated under reduced pressure and the residue was treated with aqueous HCl (30 %) until pH = 1. The aqueous phase was extracted with EtOAc. The water phase was adjusted to pH= 10 with aqueous NaOH (33 %) and was extracted with CH_2Cl_2. After drying over Na_2SO_4, the solvent was evaporated furnishing the homoallylamine **32** (yellowish oil, 1.03 g, 9.14 mmol, 92 % (84 % overall from **20**), er 99/1). ^{1}H NMR (200MHz, $CDCl_3$): δ 5.61-5.83 (m, 1H), 5.02-5.12 (m, 2H), 2.53-2.60 (m, 1H), 2.20-2.26 (m, 1H), 1.87-2.01 (m, 1H), 1.58-1.62 (m, 1H), 0.86-0.92 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 134.61, 115.54, 54.23, 37.50, 31.18, 17.50, 15.99. $[\alpha]^{27}_{589}$ –8.1 (*c* =1.04, $CHCl_3$).

(31) (yellowish oil, 78% overall from **12**. ^{1}H NMR (200MHz, $CDCl_3$): δ 7.10-7.25 (m, 5H), 5.60-5.80 (m, 1H), 5.00-5.20 (m, 2H), 3.90-4.00 (m, 1H), 2.20-2.50 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 145.85, 135.49, 128.35, 126.91, 126.34, 117.50, 55.37, 44.19.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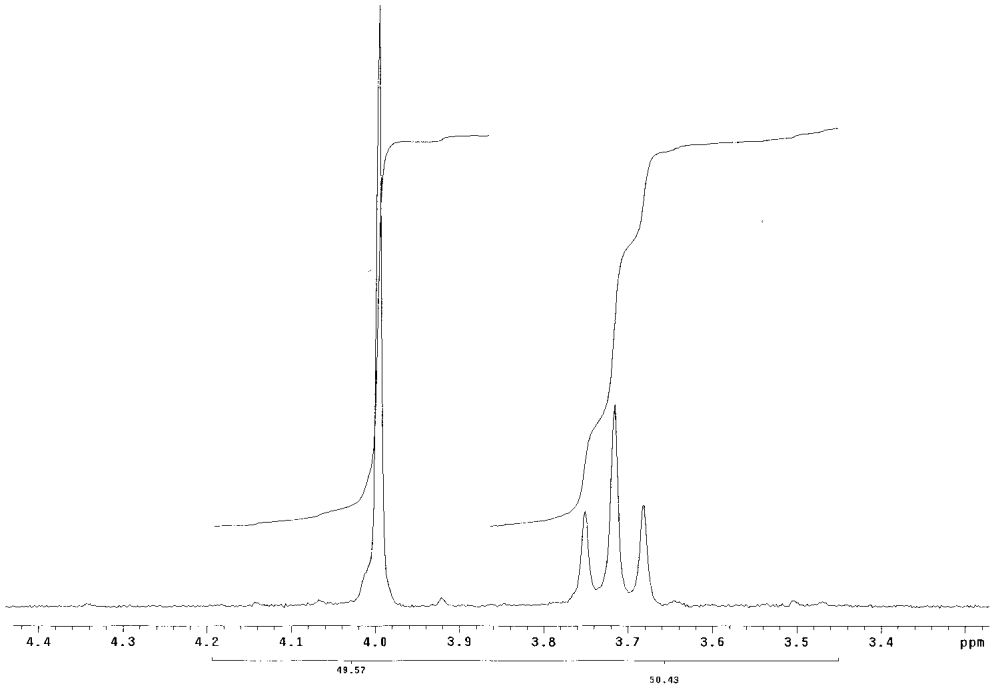
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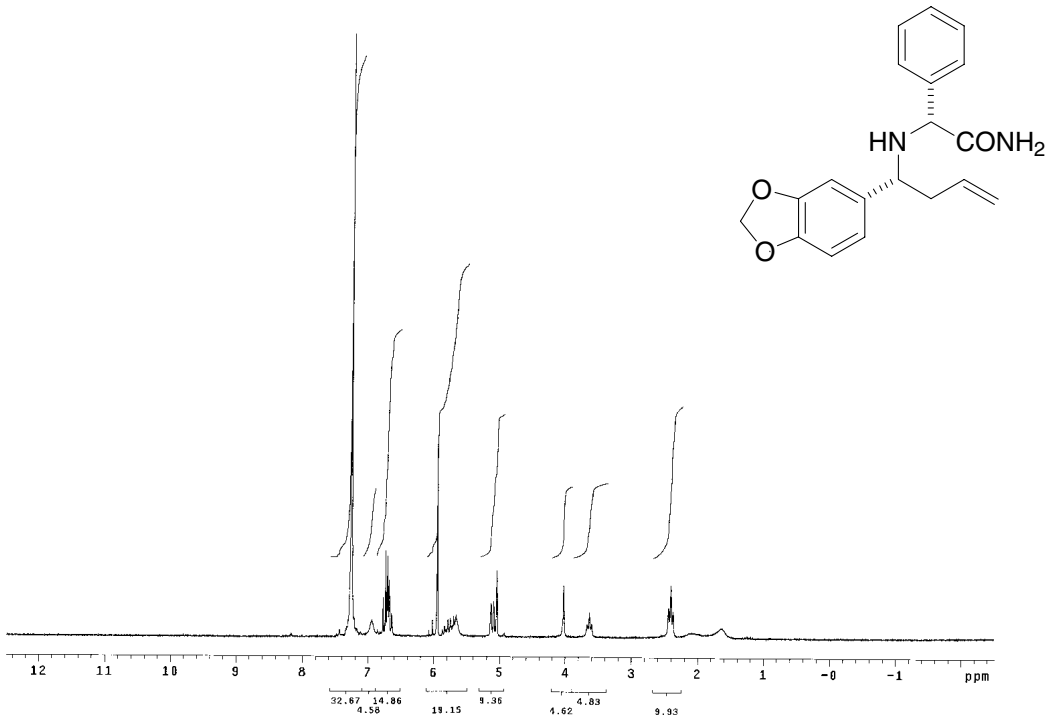
3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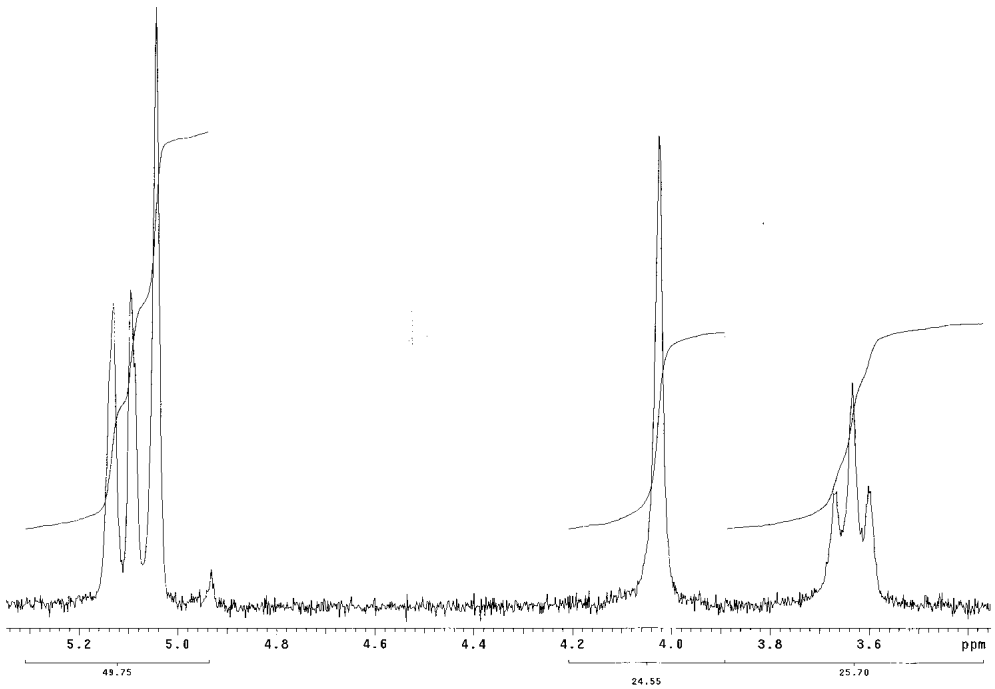
3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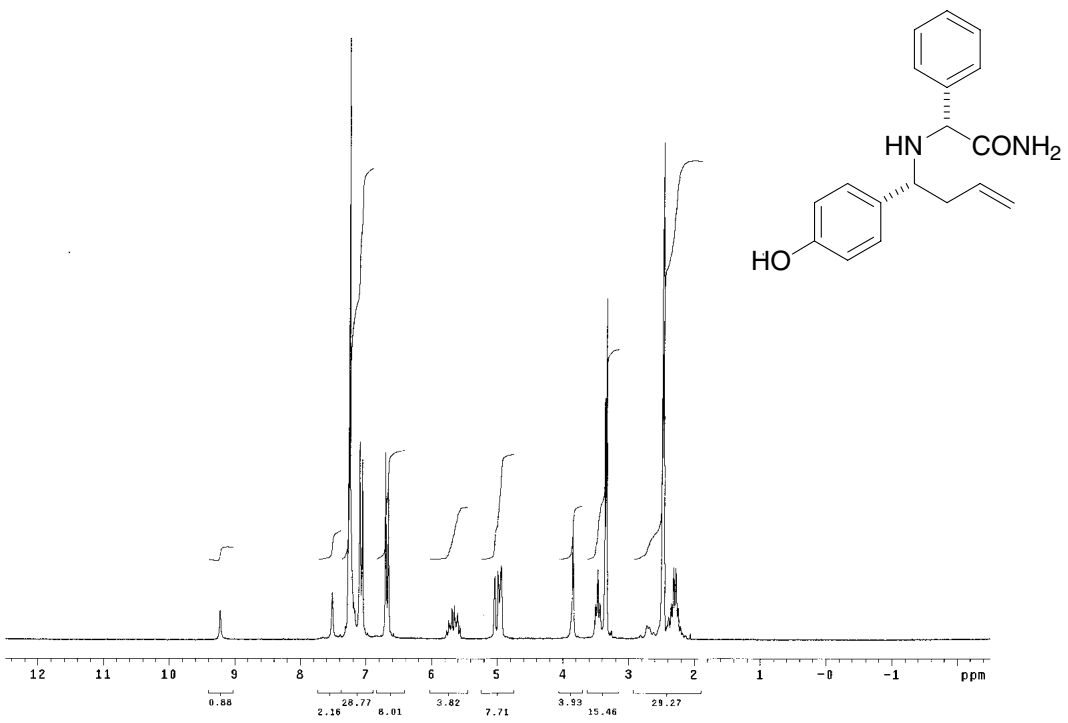
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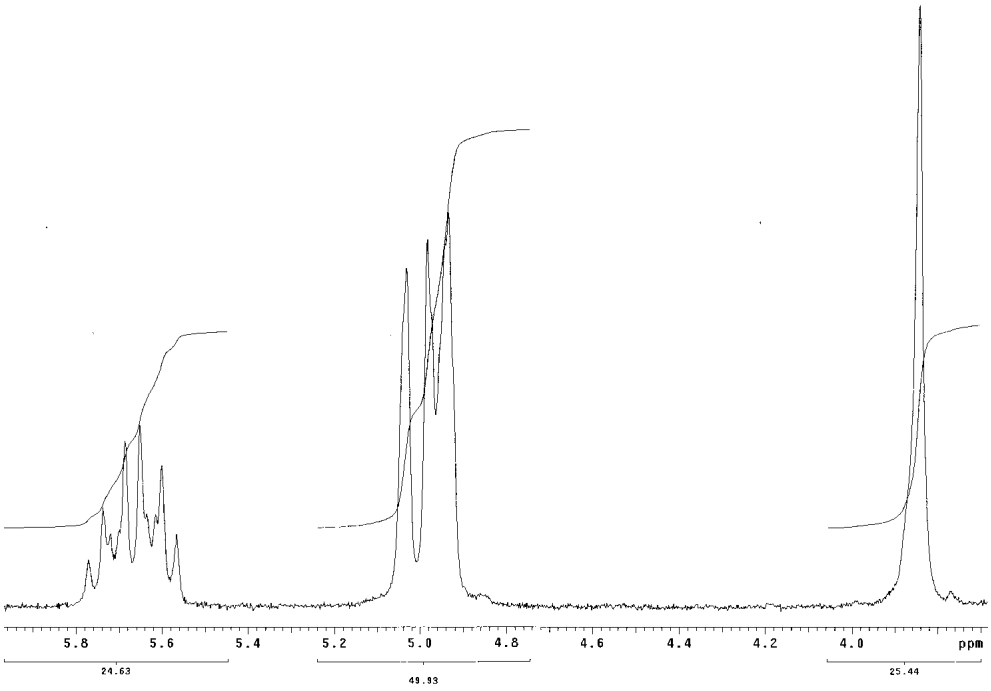
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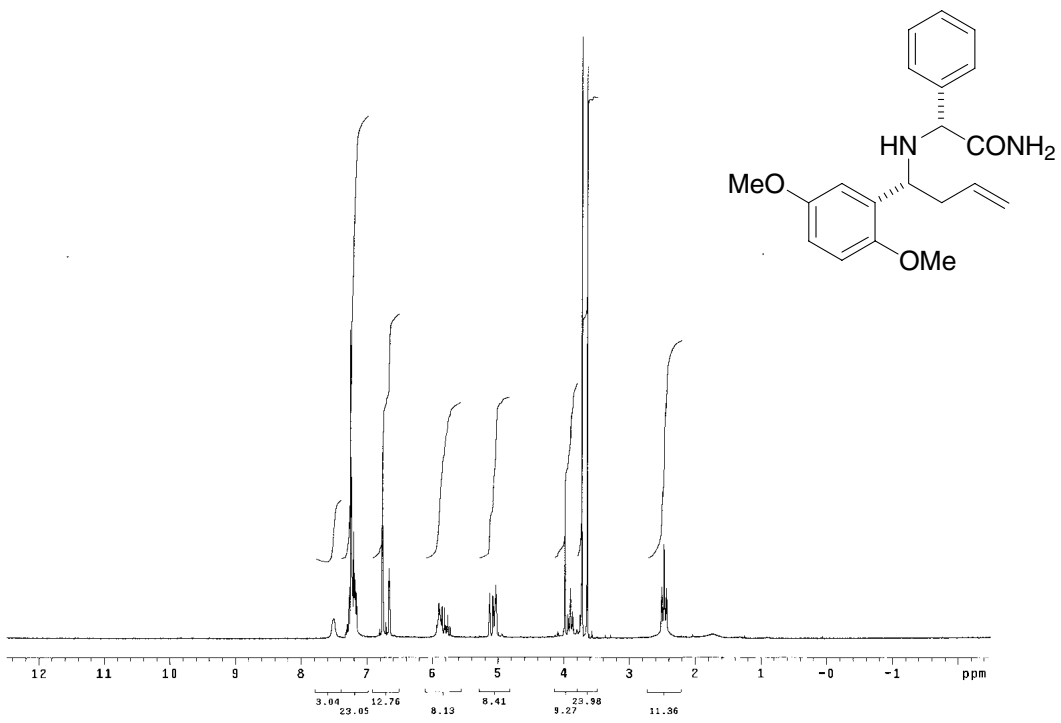
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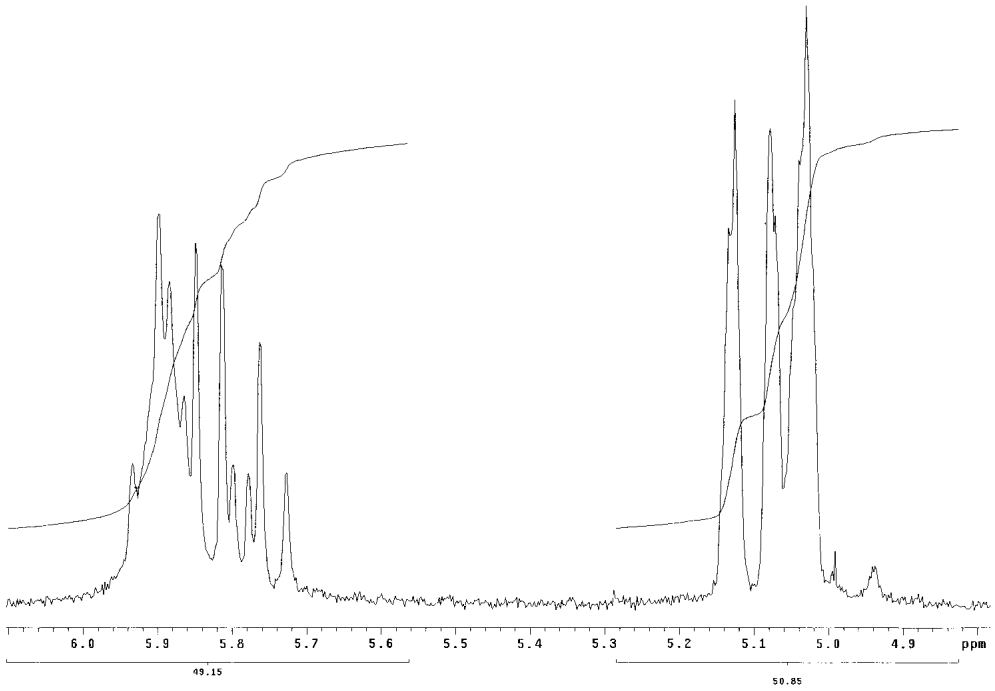
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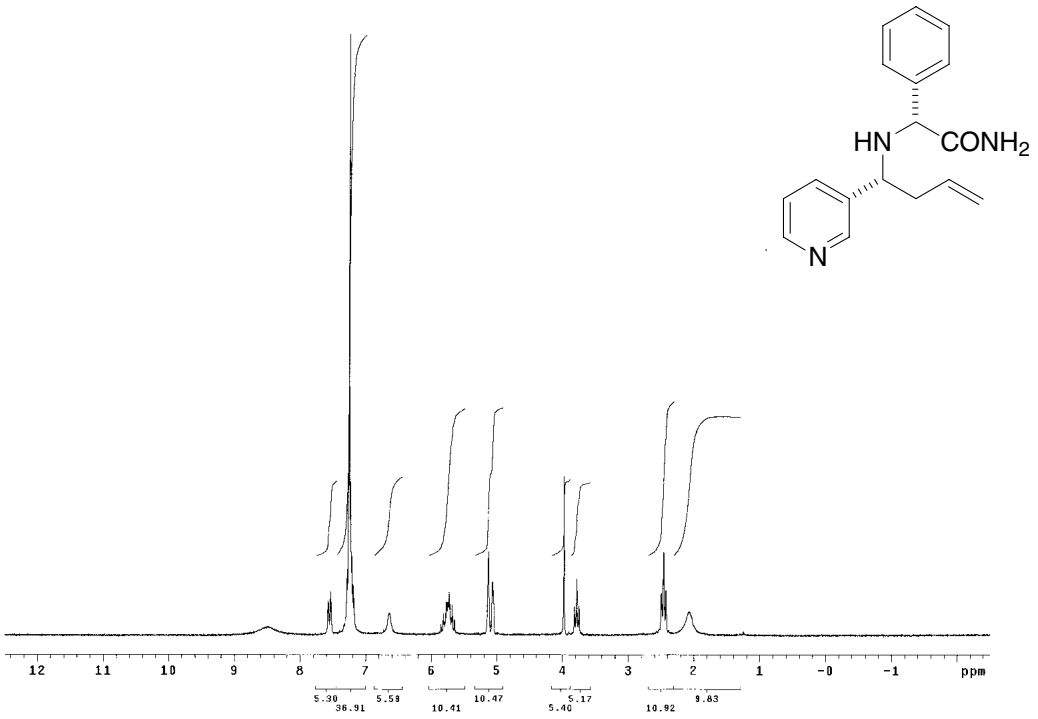
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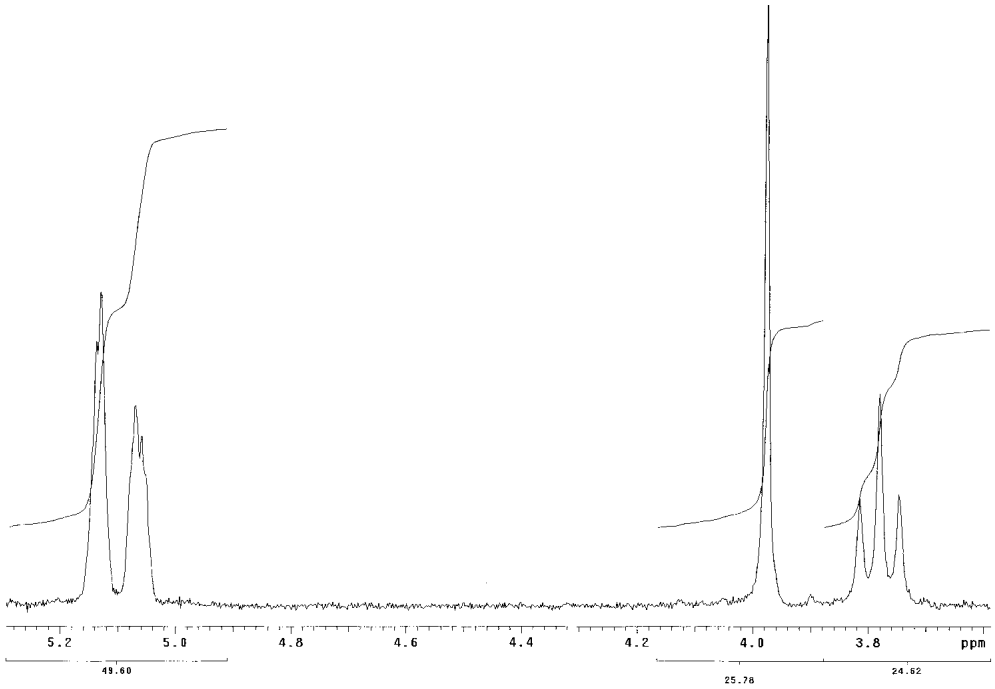
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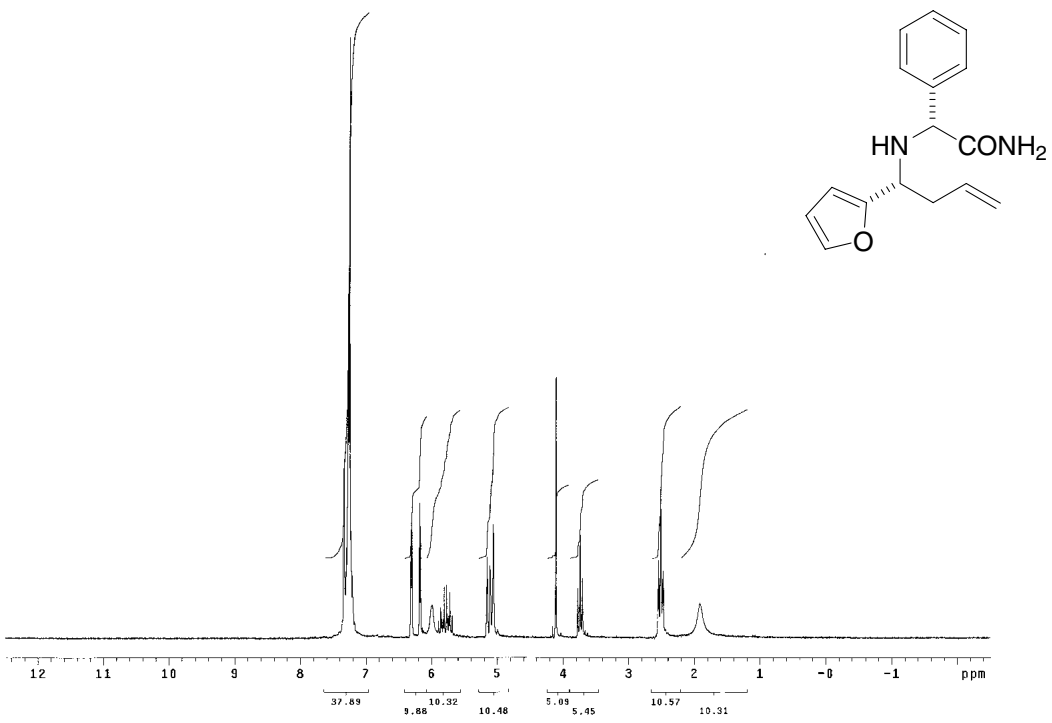
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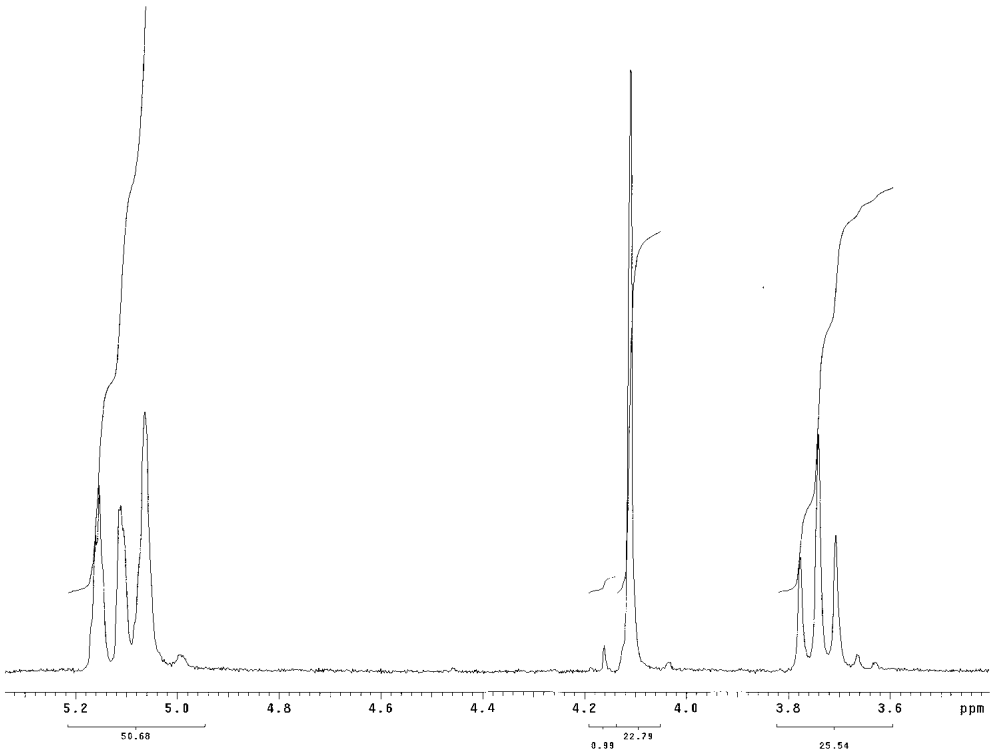
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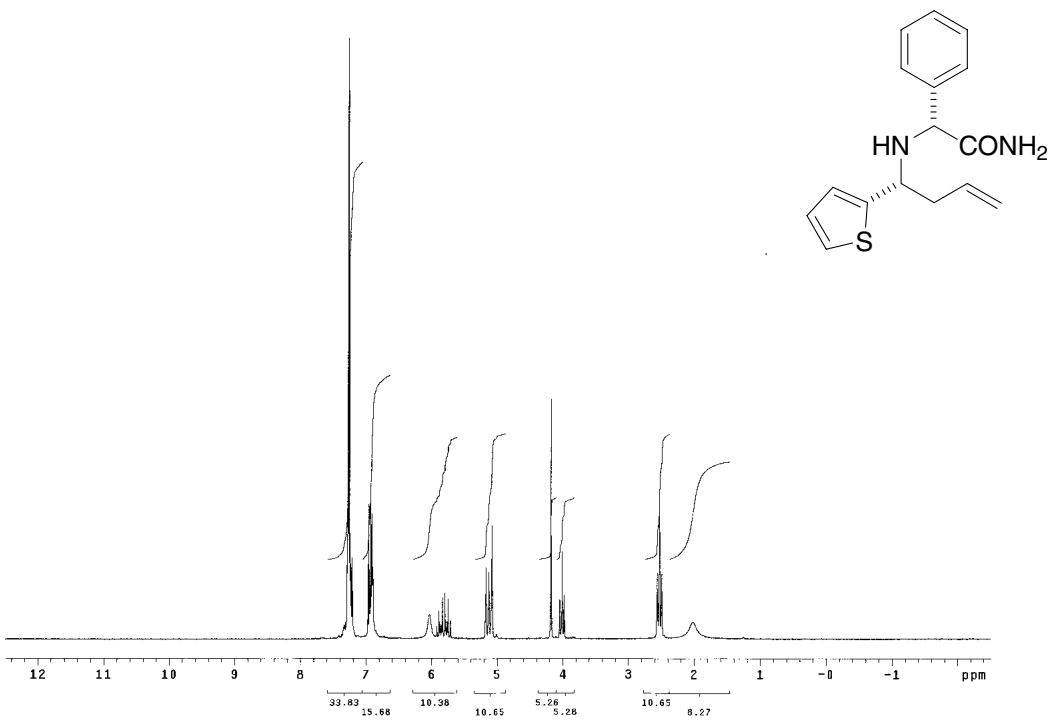
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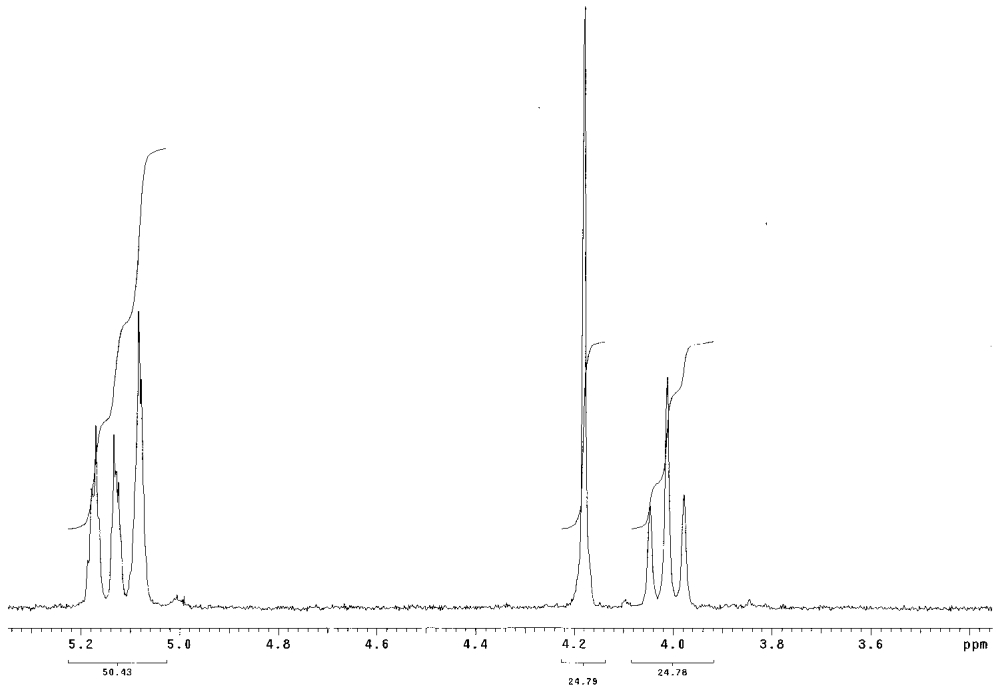
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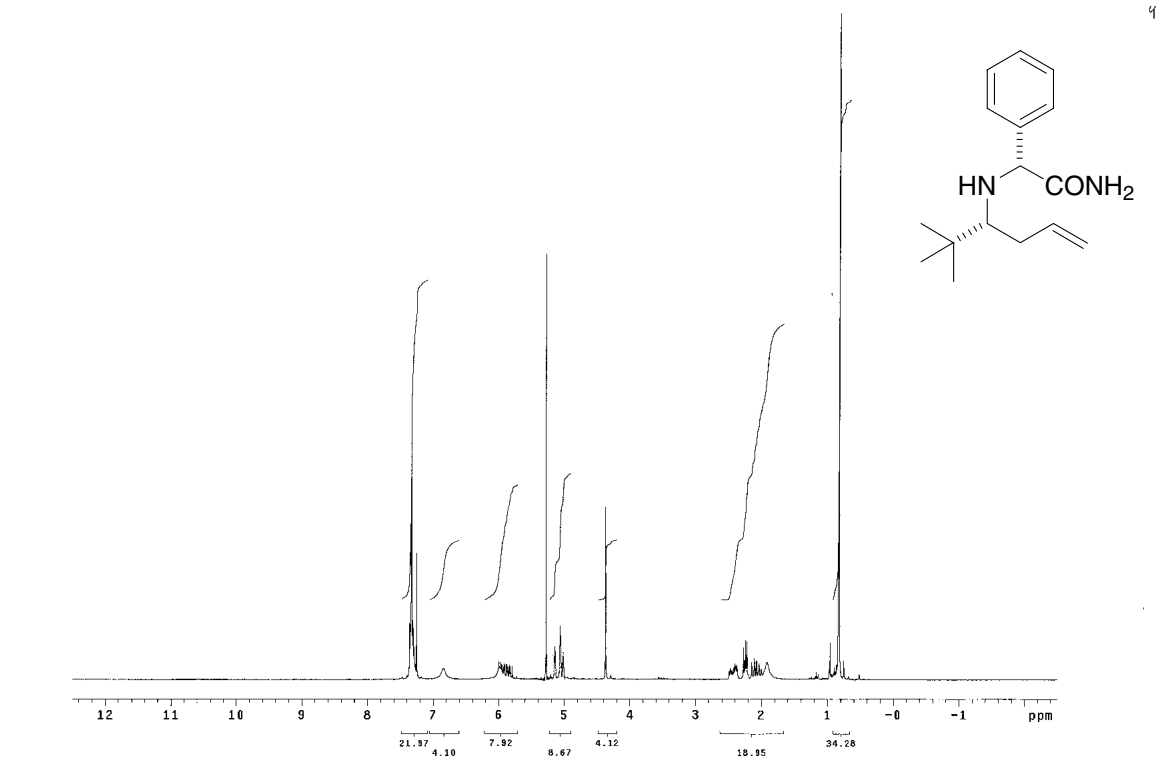
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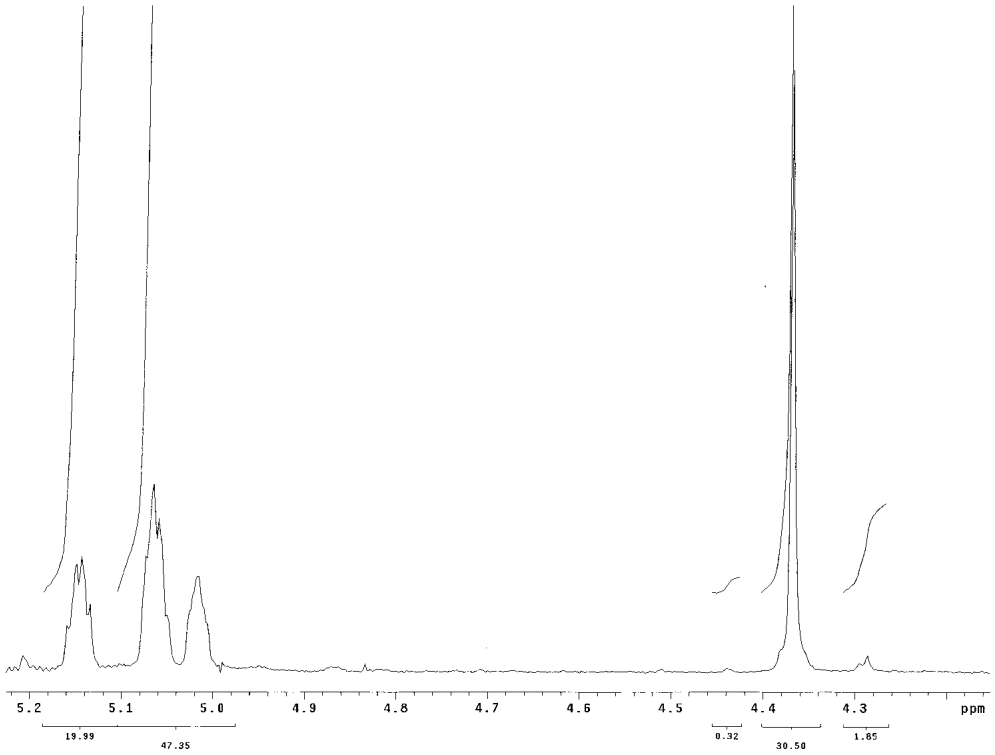
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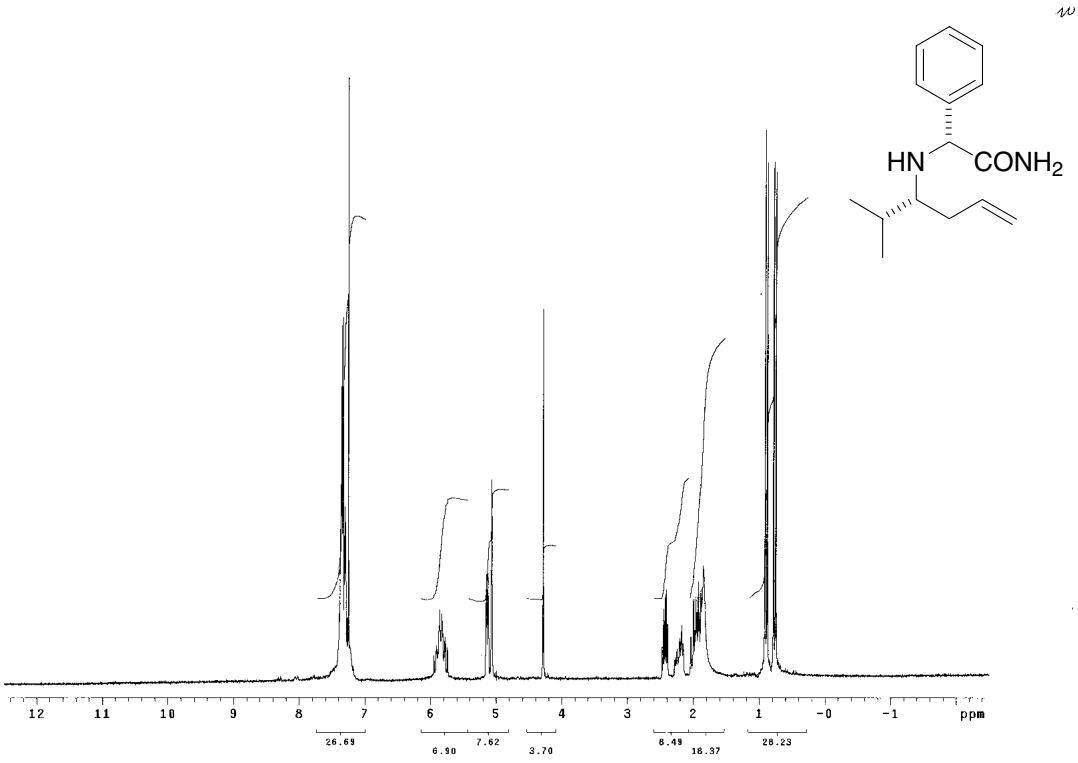
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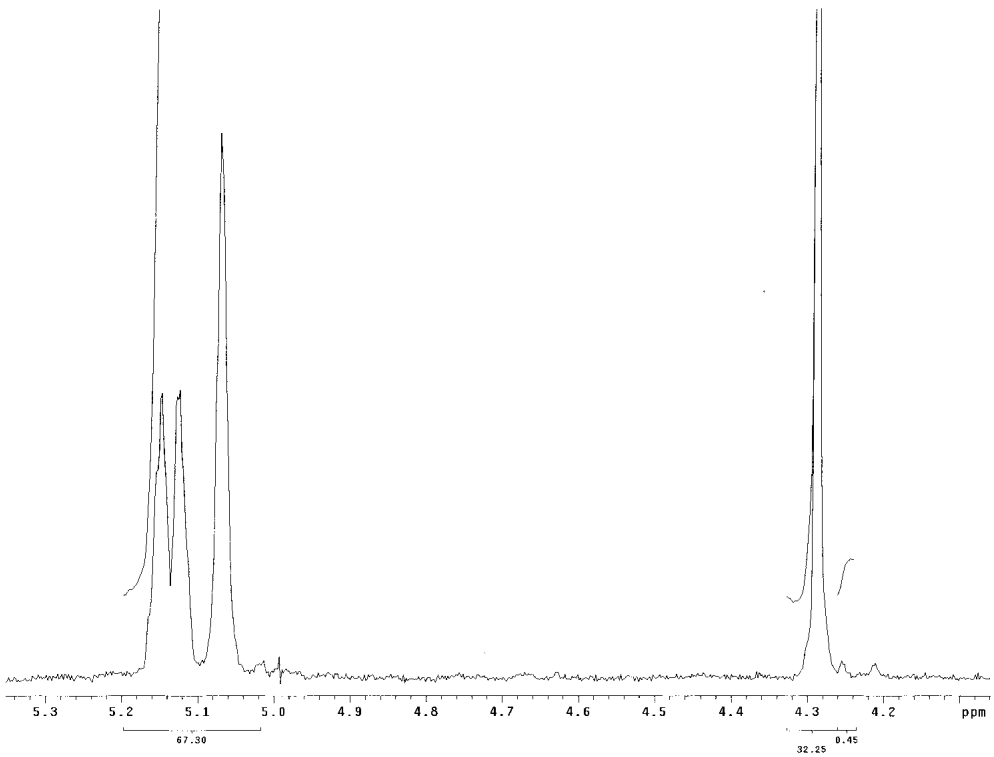
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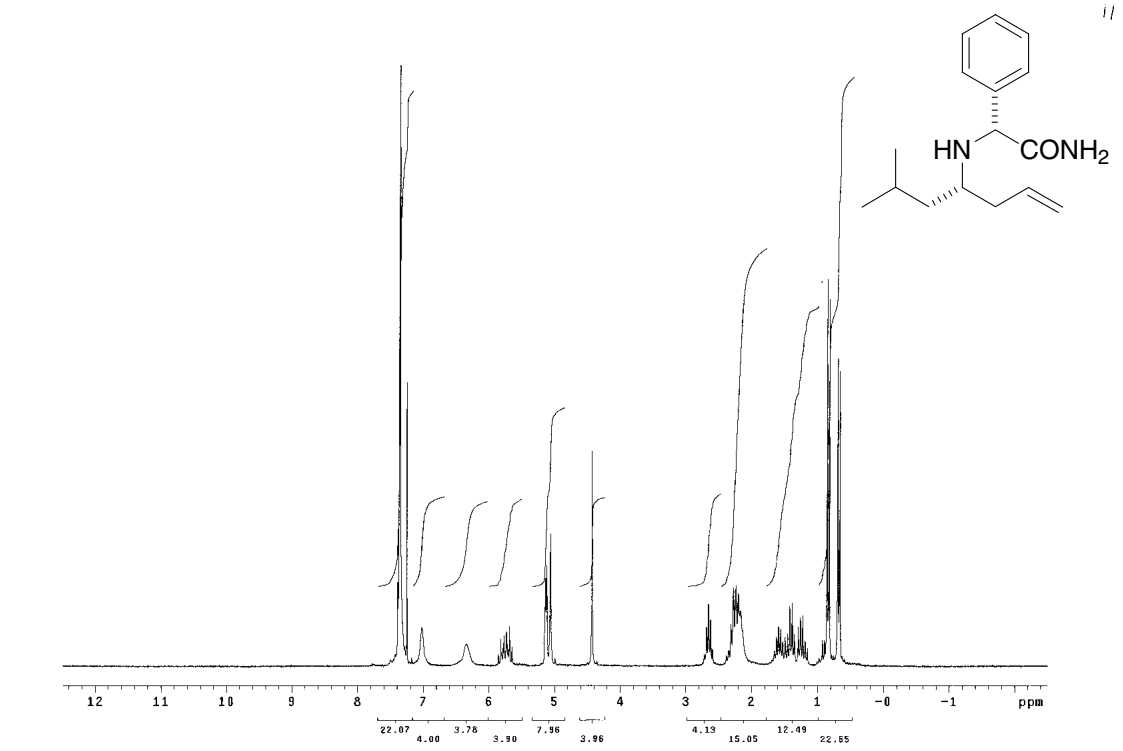
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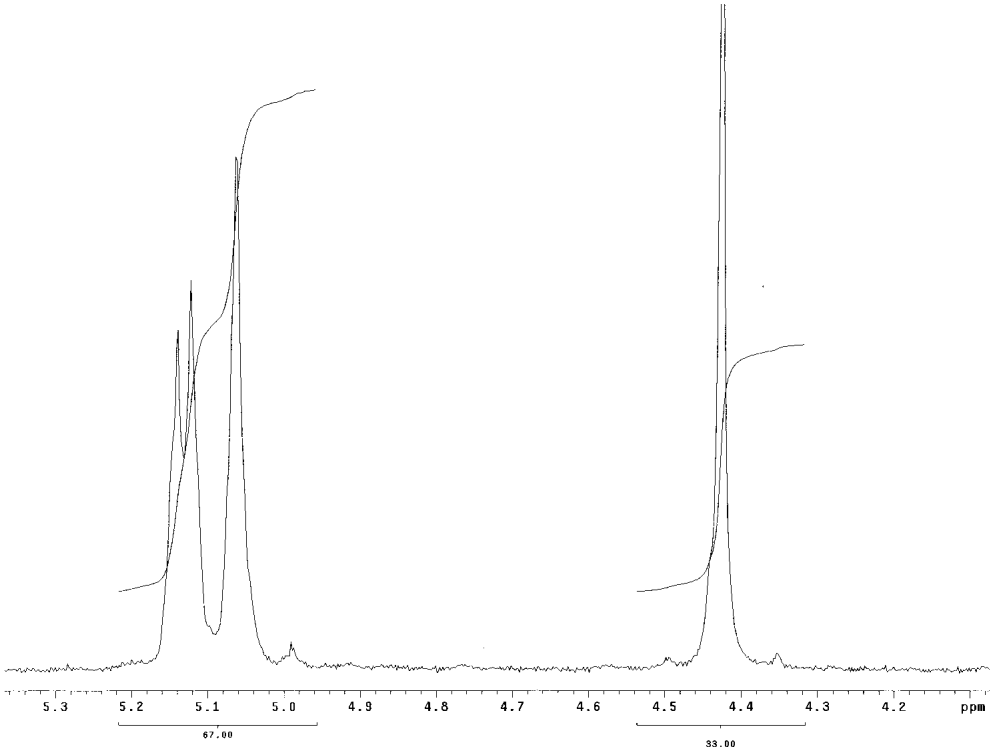
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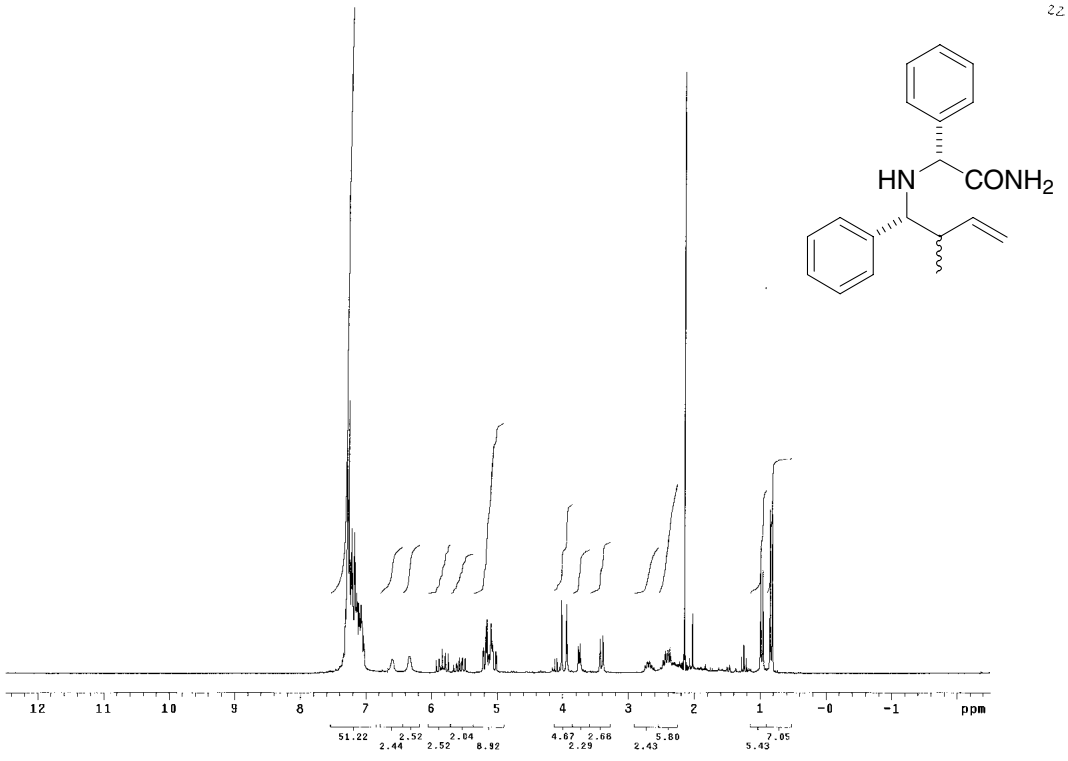
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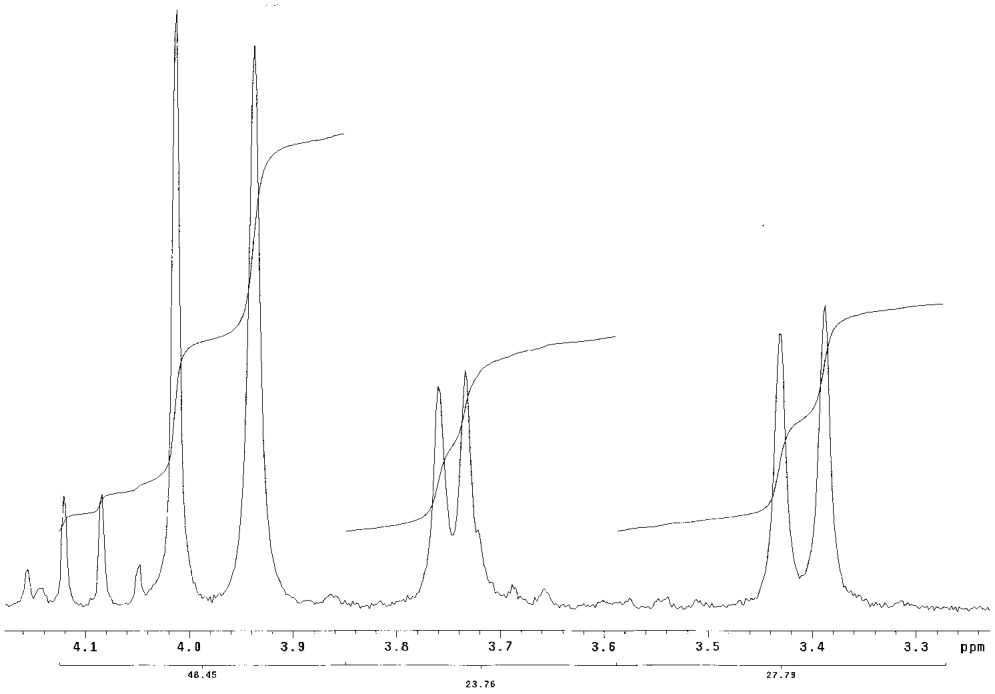
22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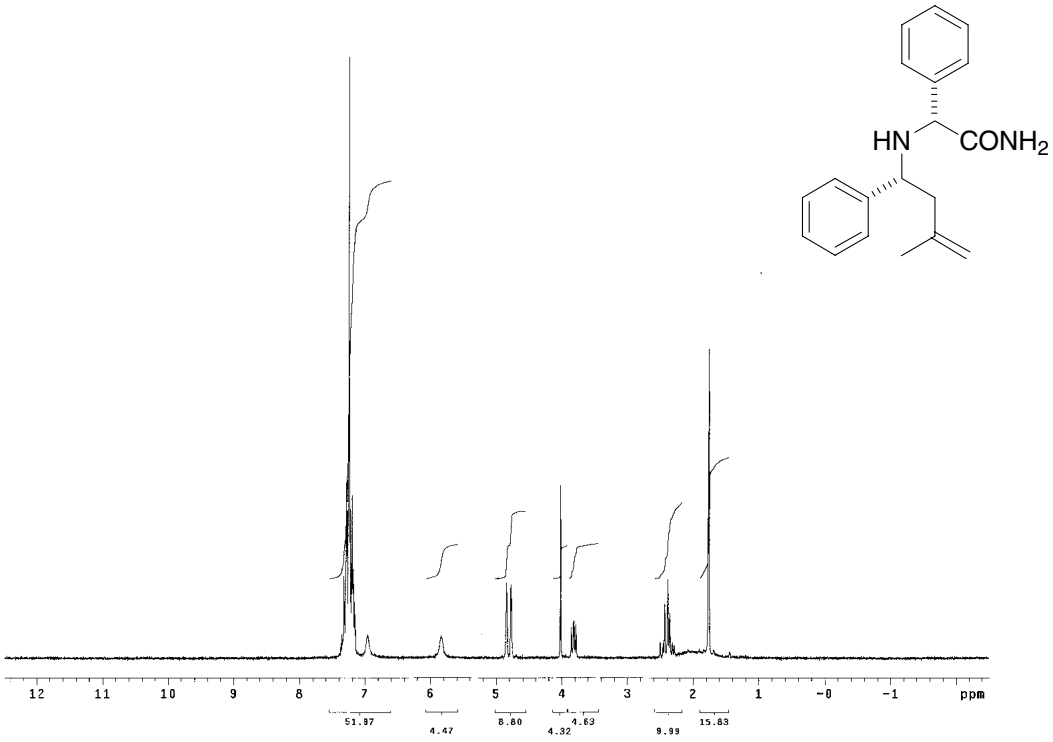
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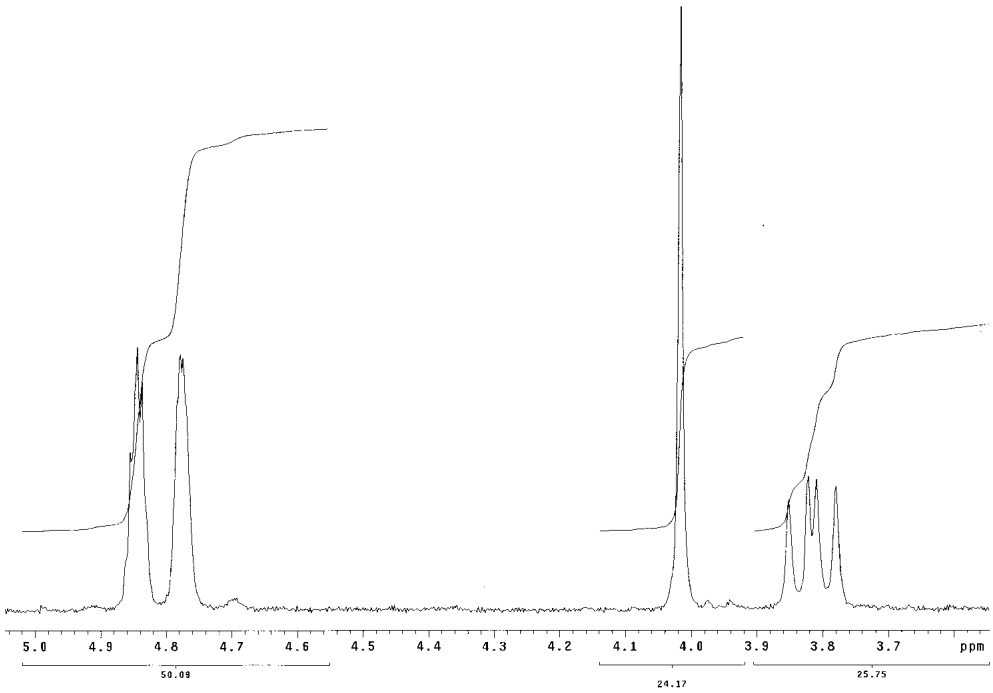
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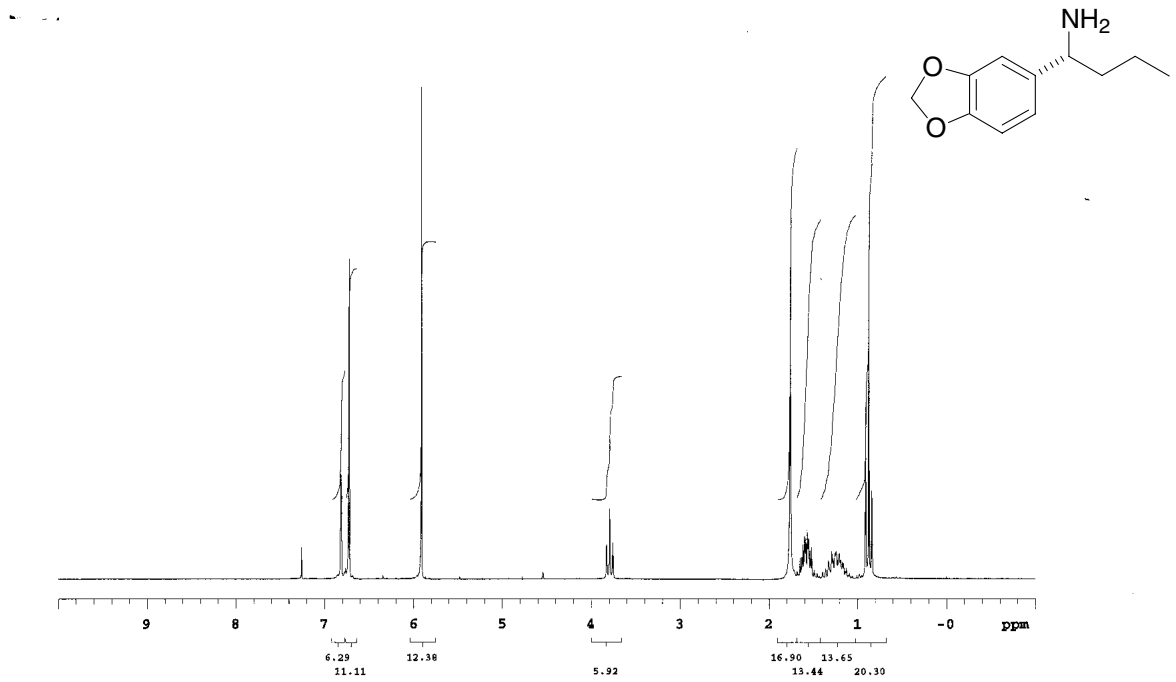
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13.65
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                                                Inj Volume : 4 µl
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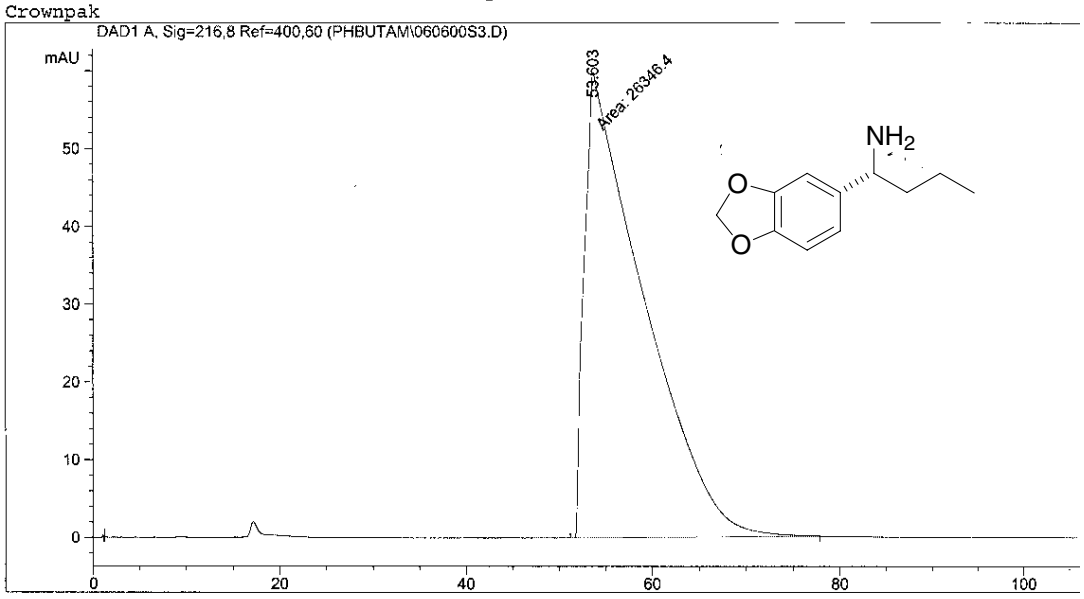
Crownpak

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==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: DAD1 A, Sig=216,8 Ref=400,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
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Totals :                  2.63464e4    59.83571

 Results obtained with enhanced integrator!
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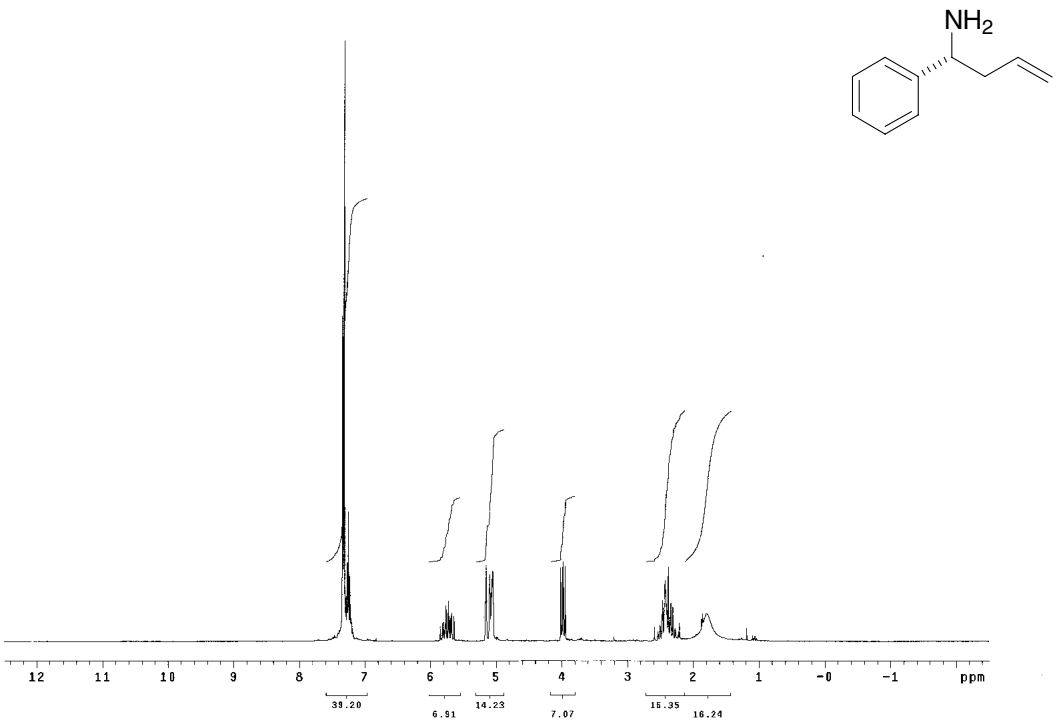
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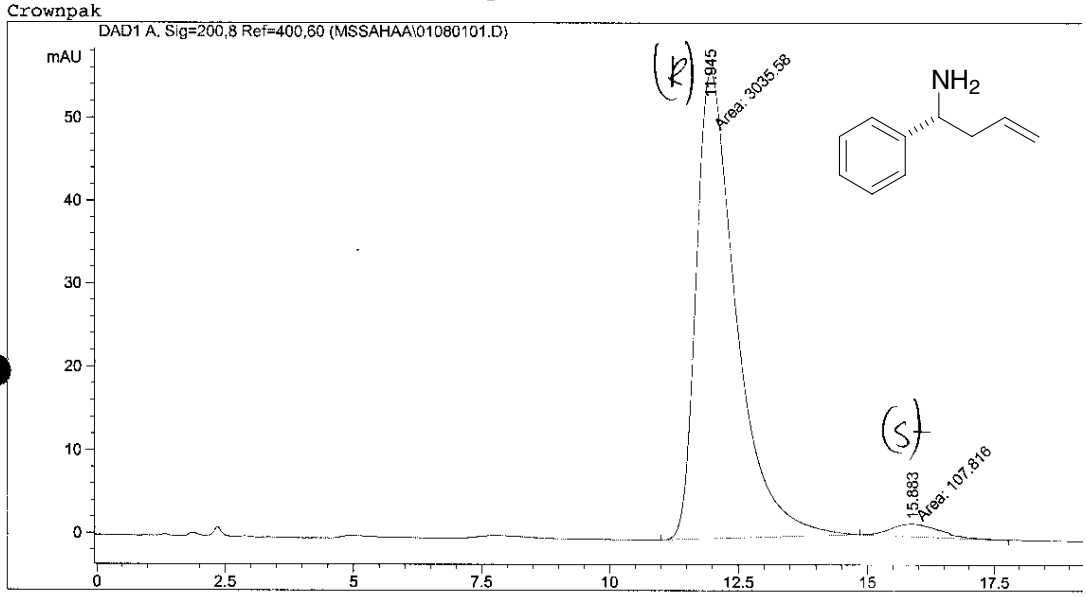
                  (modified after loading)
Crownpak
```




```
                          Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
```

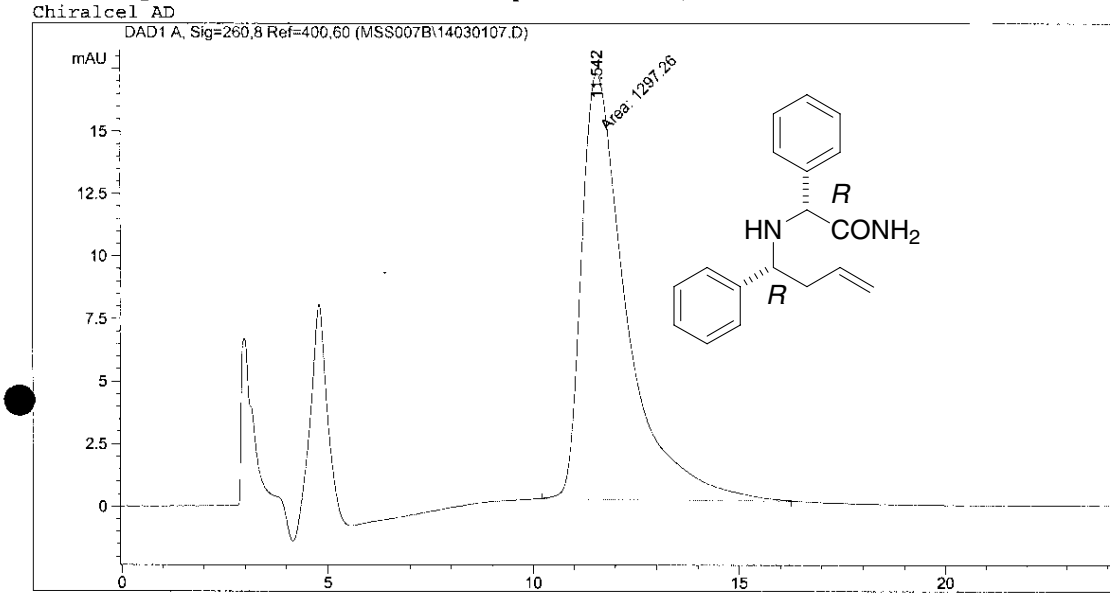
Signal 1: DAD1 A, Sig=200,8 Ref=400,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.945	MM	0.9024	3035.57544	56.06339	96.5701
2	15.883	MM	1.1450	107.81596	1.56940	3.4299
Totals :				3143.39140	57.63278	

```
 Results obtained with enhanced integrator!
                          *** End of Report ***
```

Data File C:\HPCHEM\2\DATA\MSS007B\14030107.D

```
Injection Date  : 3/14/2001 5:53:17 PM
Sample Name     :                                        Vial :  83
Acq. Operator   : M.Waalderbos/E.v.Echten
                                                  Inj Volume : 10 µl
Method          : C:\HPCHEM\2\METHODS\MSS007B.M
Last changed    : 3/14/2001 5:51:33 PM by M.Waalderbos/E.v.Echten
Chiralcel AD
```




```
                          Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: DAD1 A, Sig=260,8 Ref=400,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]    [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.542 MM    1.2708 1297.25769   17.01396 100.0000

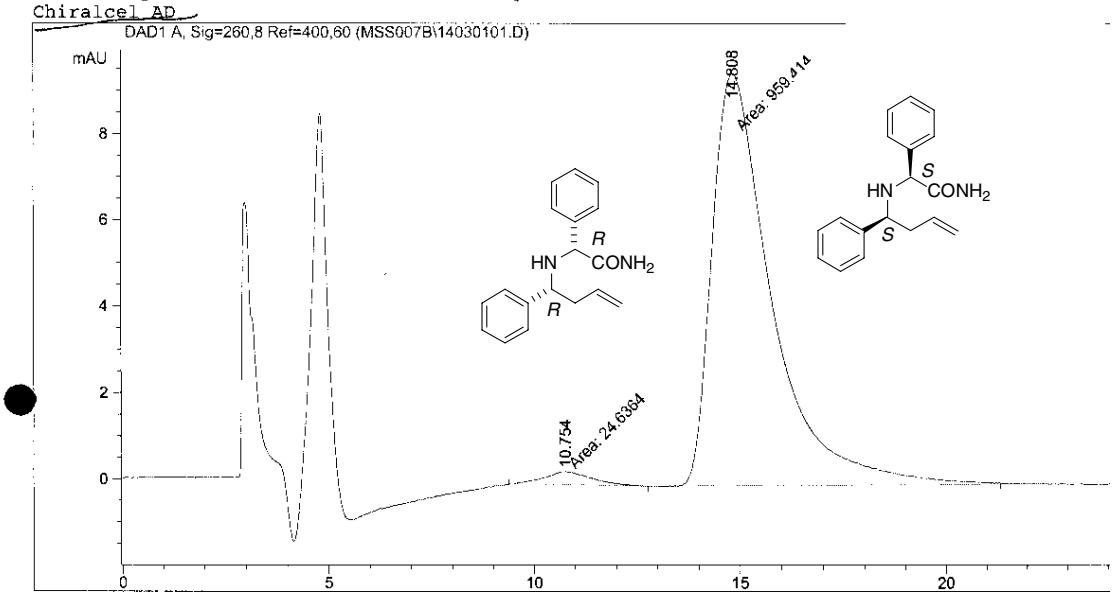
Totals :                  1297.25769   17.01396

 Results obtained with enhanced integrator!

                          *** End of Report ***
```

Data File C:\HPCHEM\2\DATA\MSS007B\14030101.D

```
==========================================================================
Injection Date  : 3/14/2001 6:21:53 PM          Seq. Line :   1
Sample Name     :                                   Vial :  84
Acq. Operator   : M.Waalderbos/E.v.Echten            Inj :   1
                                                Inj Volume : 10 µl
Method          : C:\HPCHEM\2\METHODS\MSS007B.M
Last changed    : 3/14/2001 5:51:52 PM by M.Waalderbos/E.v.Echten
Chiralcel AD
```




```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

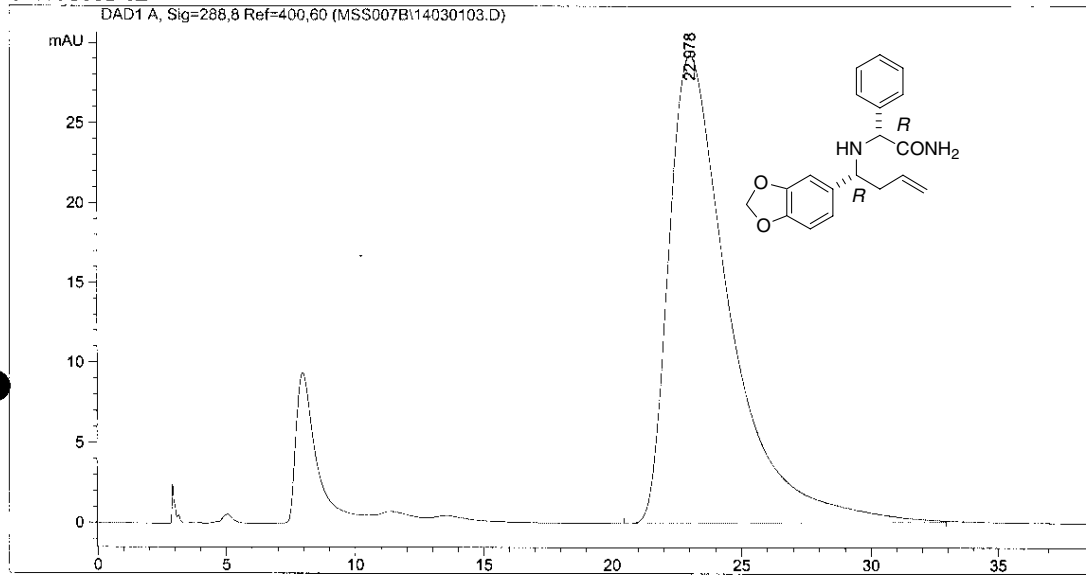
Signal 1: DAD1 A, Sig=260,8 Ref=400,60
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.754	MM	1.3234	24.63638	3.10268e-1	2.5036
2	14.808	MM	1.6755	959.41425	9.54345	97.4964
Totals :				984.05062	9.85372	

```
 Results obtained with enhanced integrator!
==========================================================================
                          *** End of Report ***
```

Data File C:\HPCHEM\2\DATA\MSS007B\14030103.D

```
==========================================================================
Injection Date  : 3/14/2001 7:30:49 PM          Seq. Line :   3
Sample Name     :                                  Vial :  86
Acq. Operator   : M.Waalderbos/E.v.Echten           Inj :   1
                                                Inj Volume : 10 µl
Method          : C:\HPCHEM\2\METHODS\MSS007C.M
Last changed    : 3/14/2001 5:54:04 PM by M.Waalderbos/E.v.Echten
Chiralcel AD
```




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: DAD1 A, Sig=288,8 Ref=400,60

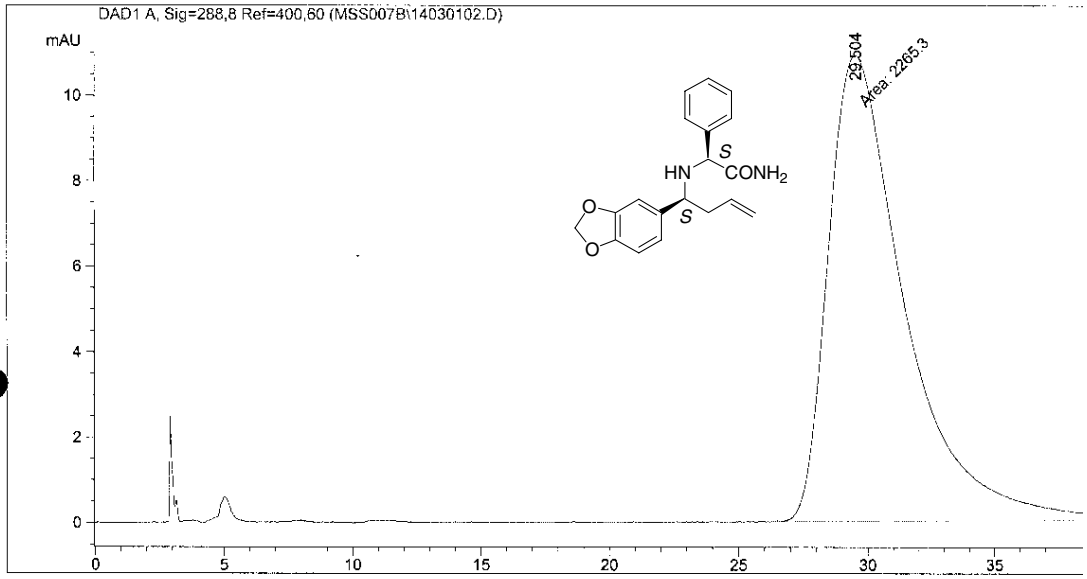
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]    [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  22.978 PB    2.4471 4807.65820   29.22644 100.0000

Totals :                  4807.65820   29.22644

 Results obtained with enhanced integrator!
==========================================================================
                        *** End of Report ***
```

Data File C:\HPCHEM\2\DATA\MSS007B\14030102.D

```
==========================================================================
Injection Date  : 3/14/2001 6:48:50 PM          Seq. Line :   2
Sample Name     :                                   Vial :  85
Acq. Operator   : M.Waalderbos/E.v.Echten            Inj :   1
                                                Inj Volume : 10 µl
Method          : C:\HPCHEM\2\METHODS\MSS007C.M
Last changed    : 3/14/2001 5:54:04 PM by M.Waalderbos/E.v.Echten
Chiralcel AD
```




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: DAD1 A, Sig=288,8 Ref=400,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]    [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  29.504 MM    3.4633 2265.29687   10.90145 100.0000

Totals :                  2265.29687   10.90145

 Results obtained with enhanced integrator!
==========================================================================
                        *** End of Report ***
```